

REMARKS

Claims 1-19 and 58 are pending in this application. Claims 2 and 20-57 are canceled without prejudice. Reexamination and reconsideration are respectfully requested.

OBJECTION TO DRAWINGS UNDER 37 CFR 1.84

The drawings were objected to as failing to comply with 37 CFR 1.84(p)(4) because reference characters "64" and "64'" (page 29, line 31-33) have allegedly both been used to designate beads. Applicants have submitted a revised FIG. 4 and revised page 29, lines 31-33. References to bead "64" and bead "64'" have been replaced with bead "64x" and bead "64y", respectively. A marked copy of FIG. 4 showing changes made has been enclosed for the Examiner's convenience.

The drawings were objected to as failing to comply with 37 CFR 1.84(p)(4) because reference character "64" has allegedly been used to designate both beads "64" (page 29, line 31) and probe (page 21, lines 21 and 23) and "74" has allegedly been used to designate both sensing field (page 30, line 7) and slit viewing field (page 30, line 11). Applicants have revised page 21, lines 21 and 23 to refer to beads "64", and page 30, line 11 has been revised to refer to a slit view of sensing field "74".

The drawings were objected to as failing to comply with 37 CFR 1.84(p)(5) because they allegedly did not include reference sign "38" mentioned in the specification (page 24, lines 14, 17 and 19). A copy of FIG. 2 as submitted on April 5, 2001 with reference sign "38" circled in red has been enclosed for the Examiner's convenience.

The drawings were objected to as failing to comply with 37 CFR 1.84(p)(5) because the following reference sign(s) were allegedly not mentioned in the description: "96" of FIGS. 6A and 6B; "122" of FIG. 9; "CPU" and "USB" of FIG. 1A. On page 33, line 10, the reference symbol "96" has been inserted after "spectrally dispersed images" and the symbol "96" is now mentioned in the description. On page 37, line 17, the reference symbol "122" has been inserted after "surface," and the reference symbol "122" is now mentioned in the specification. The specification has been revised on page 19, line 6 to recite:

"An exemplary processor is illustrated in FIG. 1A. A processor includes data input devices, a serial port connector, an interface card, a USB Connector, a

parallel port connector, an input device, a printer for hard copies, a CPU, a monitor to view data, an internal memory to store data, long term storage(Floppy, CD, Hard Disk, Cartridge, Other), image processing software, data analysis software (decodes spectra and assay signals), data processing software and database.”

The terms “CPU” and “USB” are now referred to in the description on page 19, line 6. Each of the elements are well known in the field and referred to in the above paragraph as originally described in FIG. 1A and the BRIEF DESCRIPTION OF THE DRAWINGS. Hence, no new matter has been added.

Applicants have revised drawing and the specification in response to the Examiner’s objections and request that the Examiner lift the objections to the drawings.

#### EXAMINER INTERVIEW

Applicants thank Examiners Tran and Le for the courtesy shown in a telephone interview on Wednesday, May 22, 2002. Examiner Le suggested a limitation to reciting a plurality of signals for each label. The Bawendi et al. patent was discussed, and final agreement on allowable claim language was not reached.

#### CLAIM REJECTION UNDER 35 U.S.C. §102(e)

Claims 1-7 were rejected as allegedly being anticipated by the reference of Bawendi et al. (U.S. Patent No. 6,326,144). In response to the Examiner’s suggestion, Applicant has amended independent claim 1 to include the elements of dependent claim 2 and recite a “...a plurality of signals for each label, the plurality of signals defining a plurality of wavelengths. ”

As amended, claim 1 recites a system comprising a plurality of labels generating identifiable spectra in response to excitation energy. At least some of the spectra comprise a plurality of signals for each label. Each label defines a plurality of wavelengths. The wavelengths from the spectra are intermingled. A detector simultaneously images at least some of the spectra upon a surface for identification of the labels.

In contrast, the reference of Bawendi et al. has not been shown to describe or suggest a plurality of signals for each label as recited in amended claim 1. Many figures of the

Bawendi et al. reference show labels having a single quantum dot. For example, Figure 2 of Bawendi et al. depicts a multicolored quantum dot (QD) labeled, parallel immunoassay (Col. 5, line 10). Specific-size QDs are bound to antigens (Col. 12, lines 31, 32). As depicted, QD1 labels antibody A and QD2 labels antibody B. A specific size quantum dot has a specific band gap and secondary emission frequency, so that "a plurality of signals for each label" as recited in claim 1 has not been shown in the reference.

As set forth above the reference of Bawendi et al. has not been shown to describe or suggest a plurality of signals for each label as recited in claim 1. Therefore, claim 1 is patentable over the reference of Bawendi et al.

For reasons similar to those set forth with regard to independent claim 1, independent claim 58 is patentable over the reference of Bawendi et al. Claims 3-19 depend from claim 1 and are allowable as depending from allowable an allowable claim and reciting additional novel combinations of elements.

Applicants will address the provisional non-statutory double-patenting rejections when the Examiner has determined that present application is otherwise in condition for allowance.

### CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

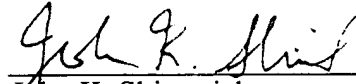
Attached is a marked up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE". Substitute drawing sheets have been enclosed showing the changed made in red, together with a clean version of each sheet.

STEPHEN A. EMPEDOCLES et al.  
Application No.: 09/827,076  
Page 9

PATENT

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



---

John K. Shimmick  
Reg. No. 44,335

TOWNSEND and TOWNSEND and CREW LLP  
Two Embarcadero Center, 8<sup>th</sup> Floor  
San Francisco, California 94111-3834  
Tel: (415) 576-0200 // Fax: (415) 576-0300  
JKS:nap  
PA 3231185 v1

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

Please substitute the following paragraphs where indicated within the specification. A version showing changes has been submitted herewith under the heading "VERSION WITH MARKINGS TO SHOW CHANGES MADE"

Please replace the second paragraph on page 29, with the following ( so as to replace "probe 64 has" with --beads 64 have-- on line 21 and "probe 64" with --beads 64-- on line 23):

As described above, it will often be advantageous to include a plurality of different spectrally labeled beads within a fluid. These labeled beads will often be supported by the surrounding fluid, and/or will be movable with the fluid, particularly in high-throughput multiplexed bead-based assays. Optionally, the beads may have a size sufficient to define a suspension within the surrounding test fluid. In some embodiments, the beads may comprise a colloid within the test fluid. In some embodiments, beads 64 may be movably supported by a surface of a vessel containing the test fluid, for example, being disposed on the bottom surface of the vessel (where **[probe 64 has]** beads 64 have a density greater than that of the test fluid). In other embodiments, the beads may be affixed to a support structure and/or to each other. Still further alternatives are possible, such as for **[probe]** beads 64 to be floating on an upper surface of the test fluid, for the bead or beads to be affixed to or disposed between cooperating surfaces of the vessel to maintain the positioning of the bead or beads, for the bead or beads to be disposed at the interface between two fluids, and the like.

Please replace the last paragraph started on page 29 with the following (so as to replace "bead 64" with "bead 64x", "bead 64' " with "bead 64y" and "individual bead 64" with --individual bead 64x-- respectively):

As was described above, it will often be advantageous to include numerous beads 64 within a single test fluid so as to perform a plurality of assays. Similarly, it will often be

advantageous to identify a large number of fluids or small discreet elements within a single viewing area without separating out each spectral label from the combined labeled elements. As illustrated in Fig. 4, the dispersed spectral image 68 of bead [64] 64x upon sensor 56 will depend on both the relative spectra generated by the bead, and on the position of the bead. For example, bead [64'] 64y is imaged onto a different portion 68' of sensor 56, which could lead to misinterpretation of the wavelengths of the spectra if the location of bead [64'] 64y is not known. So long as an individual bead [64] 64x can be accurately aligned with the imaging optics 58 and sensor system 66, absolute spectral information can be obtained. However, as can be understood with reference to Fig. 5A, a plurality of beads 64 will often be distributed throughout an area 70.

Please replace the first full paragraph on page 30 with the following (so as to replace "slit viewing field 74" with --slit view of sensing field 74--):

To ensure that only beads 64 which are aligned along an optical axis 72 are imaged onto sensor 56, aperture 62 restricts a sensing field 74 of the sensing system. Where sensor 56 comprises an areal sensor such a charge couple device (CCD), aperture 62 may comprise a slit aperture so that spectral wavelengths  $\lambda$  can be determined from the position of the dispersed images 68 along a dispersion axis of wavelength dispersive element 54 for multiple beads 64 distributed along the slit view of sensing [viewing] field 74 along a second axis y, as can be understood with reference to Fig. 5B. Absolute accuracy of the spectral readings will vary inversely with a width of aperture slit 62, and the number of readings (and hence total reading time) for reading all the beads in area 70 will be longer as the slit gets narrower. Nonetheless, the beads 64 within the two-dimensional area 70 may eventually be read by the system of Figs. 5A and 5B with a scanning system which moves the slit relative to beads 64 (using any of a variety of scanning mechanisms, such as movable mirrors, a movable aperture, a flow of the beads passed a fixed aperture, a movement of the surface of the vessel relative to the aperture, or the like).

Please replace the first paragraph on page 33 with the following (so as to add the reference number --96-- after "spectrally dispersed images" at the end of line 10):

Correlation of the positioning image 88 with the spectrally dispersed image 68 can be understood with Figs. 6A through 6C. Positioning image 88 generally indicates positions of beads 64 within sensing field 81, while spectrally dispersed image 68 reflects both the position and spectral wavelengths of each signal within the spectra generated by beads 64. Using an accurately calibrated system, analyzer 90 can determine the absolute wavelengths of a particular dispersed image 96a by identifying the associated bead position 64a, particularly where beads 64 do not overlap along the *y*-axis. As can be understood with reference to Figs. 6B and 6C, correlation of beads' locations and spectrally dispersed images 96 may be facilitated by including a calibration signal 40c within at least one of the spectra generated by a bead. Such calibration signals will often be included in at least some of the bead spectra, optionally being included in each bead spectrum. Where the calibration signal wavelength is known, the location of the associated bead along the *x*-axis can be determined from the location of the calibration signal energy within the dispersed image 68 from the diffracting characteristics of wavelength dispersive element 54.

Please replace the third full paragraph on page 37 with the following (so as to add the reference number --122-- after "image the sensing field upon a surface" on line 17):

To allow scanning/imaging system 120 to detect relatively low-intensity signals within the two-dimensional sensing field 81, optics 58 image the sensing field upon a surface 122 of sensor 56. A spectral filter 128 selectively transmits marker signals 102 to sensor 56 of the detector, thereby avoiding saturation from the relatively high-intensity spectral label signals. Using our simple marker/label separation scheme illustrated in Fig. 8, filter 128 may comprise a dichroic filter which selectively transmits the marker signals within second range 112b. Clearly, more complex filtering and signal separation arrangements are possible. Regardless, as numerous beads 64 within two-dimensional sensing field 81 can have their assay markers detected simultaneously, a relatively long integration time may be employed without adding excessively to the overall sensing time.

Please insert the following new paragraph before the heading Fabrication of Labeled Beads on page 19 of the specification as follows.

--An exemplary processor is illustrated in FIG. 1A. A processor includes data input devices, a serial port connector, an interface card, a USB Connector, a parallel port connector, an input device, a printer for hard copies, a CPU, a monitor to view data, an internal memory to store data, long term storage (Floppy, CD, Hard Disk, Cartridge, Other), image processing software, data analysis software (decodes spectra and assay signals), data processing software and database.--

IN THE CLAIMS:

Please amend claims 1, 3, 12, and 17; please cancel claims 2 and 20-57; and please add new claim 58 as follows.

- 1                   1. (Amended) A system comprising:  
2                   a plurality of labels <sup>each</sup> generating identifiable spectra in response to excitation  
3 energy, wherein at least some of the spectra comprise a plurality of signals for each label, the  
4 plurality of signals defining a plurality of wavelengths, the wavelengths from the spectra being  
5 intermingled; and  
6                   a detector simultaneously imaging at least some of the spectra upon a surface for  
7 identification of the labels.

*Please cancel claim 2.*

- 1                   3.        (Amended) The system of claim 1, wherein the labels [**comprises**]  
2 comprise at least one semiconductor nanocrystal.

- 1                   12.     (Amended) The system of claim 1, further comprising a spatial position  
2 indicator to identify label positions within [**the**] a sensor field of the detector, wherein the  
3 detector senses relative spectral data.

- 1                   17.     (Amended) The system of claim 1, wherein [**at least some of the**  
2 **spectra comprise a plurality of signals,**] the detector [**further comprising**] comprises means  
3 for distributing the signals across a sensor in response to wavelengths of the signals and positions



4 of the labels in [the] a sensor field, the distributing means disposed between the sensing field and  
5 the sensor.

Please cancel claims 20-57.

1 58. (New) A system comprising:  
2 a plurality of labels generating identifiable spectra in response to excitation  
3 energy, wherein at least some of the spectra comprise a plurality of signals for each label;  
4 a detector simultaneously imaging the spectra upon a surface of a sensor for  
5 identification of the labels, the detector comprising a dispersion member dispersing wavelengths  
6 of the spectra across the surface of the sensor; and  
7 a spatial position indicator to identify label positions within a sensor field of the  
8 detector.